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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,728	05/08/2002	Audrey Goddard	P3230R1C001-168	1383

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EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,728	GODDARD ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,11-14 and 16-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,11-14 and 16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/26/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix A*.

DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn as indicated by the petition decision mailed 1/5/2006.

2. Amendments and response filed 9/26/2005 is acknowledged. Claims 19 and 30 have been amended. Claims 4-6, 11-14 and 16-31 are pending and under examination in the Instant Application.

3. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

4. The Office acknowledges the submission of the IDS dated 9/26/2005.

5. The pending claim rejections under 35 USC § 102(e) is withdrawn.

35 USC § 112, first paragraph – Enablement

6. The rejection of claims 4, 5, 14 and 16-31 under 35 U.S.C. 112, first paragraph, because the specification does not enable one of skilled in the art to which it pertains, or with which it is most closely connected, to make and/or use the invention commensurate in scope with these claims is maintained for the reasons of record.

The reasons for this rejection under 35 U.S.C. § 112, first paragraph, are set forth in the previous Office Action 07 February 2005 and 25 July 2005. Specifically, SEQ ID NO: 113 fragments, polynucleotides that are 95 or 99% identical to such or to the full-length cDNA, and polynucleotides which hybridize to any of the above are not enabled because there is no structural or functional information provided in the

specification which correlates these molecules to those which would be more "highly expressed in normal stomach compared to stomach tumor". In addition, the lack of direction/guidance presented in the specification regarding which variants of polynucleotides of SEQ ID NO: 113 encoded proteins would retain the recited property, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, the absence of working examples directed to variants and the breath of claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Although Applicants have amended the claims to assert that the nucleic acid is more highly expressed in normal stomach tissues compared to stomach tumor tissue, there is no way of knowing which, if any, variants would have the same property of higher expression in the specific tissue. There is no nexus between the degree of homology and the property of being expressed in normal stomach tissue to a greater degree that in cancer. Until one identifies a particular variant that demonstrates a higher expression or not, one of skilled in the art would not know the expression profile of the variant. The invention is not one of making a variant with conserved structural regions, wherein the conserved structure provides for a particular biological activity. In the instant case, the claims do not require any function. The property recited has only been shown for SEQ ID NO: 113 and no other molecules related to SEQ ID NO: 113 have been described. One of ordinary skill in the art has no expectation that any variant, which is made, will also have the property of "higher expression in normal stomach tissue compared to stomach tumor". While one could screen for these molecules,

screening is not "making" and the specification fails to teach how to make a molecule, which is "higher expression in normal stomach tissue compared to stomach tumor" with any reasonable expectation of success, absent evidence to the contrary.

Applicants on page 6 of the response filed 9/26/2005 assert that the claimed nucleic acids are enabled, as one of skill in the art would know how to make and use them. This argument has been fully considered but not found to be persuasive because the biological activities described in the specification are to the full length polypeptide of SEQ ID NO: 114. However, polynucleotides of SEQ ID NO: 113 fragments or nucleotides encoding polypeptide of SEQ ID NO: 114 or the full-length cDNA deposited as ATCC accession number 203285, nor polynucleotides which hybridize to any of the above or complement thereof are not described because there is no structural or functional information provided in the specification. In addition, the lack of direction/guidance presented in the specification regarding which variants of polynucleotides of SEQ ID NO: 113 encoded proteins would retain the recited property, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, the absence of working examples directed to variants and the breath of claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Although, Applicants argue that the specification describes methods for determining the percent identity between two disclosed sequences (see page 6 of the response), there is no nexus established between the percent identity of the sequences and the recited property of the variant PRO1446 sequences. In addition, even if the

specification teaches methods to make changes to the polynucleotides it does not teach which sequences are crucial to retain the biological activities of PRO1446. In the absence of further guidance, it would require undue experimentation of the skilled artisan to make and/or use the claimed invention in its full scope. For example, there is no guidance with respect to which polynucleotide sequences are required for over expression in stomach. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications of the polynucleotides contemplated and yet retain the recited property of the PRO1446 of polynucleotides claimed.

The Office agrees with Applicants argument that the PTO did not provide support for "hybridization under moderately stringent conditions would yield nucleic acid molecules that are structurally unrelated", therefore it is withdrawn (see page 7 of the response). However, the specification is not enabling for nucleic acids having at least 95% sequence identity to those nucleic acids hybridizing to the complement of a nucleic acid of SEQ ID NO: 113 at higher stringency.

Accordingly, the disclosure fails to enable such a myriad of the claimed nucleic acid molecules that not only vary substantially in length but also in nucleic acid composition and to provide any guidance to one skilled in the art on how to make and use the claimed genus of nucleic acid molecule. Thus, it would require undue

experimentation for one skilled in the art to make and use the claimed genus of the molecules embraced by the instant claims. In re *Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Therefore, the rejections of record are maintained.

35 USC § 112, first paragraph – Written Description

7. Claims 4, 5, 7, 14 and 16-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention is maintained.

The reasons for this rejection under 35 U.S.C. § 112, first paragraph, are set forth in the previous Office Action 07 February 2005 and 25 July 2005. Briefly, the Applicants were not in possession of all or a significant number of polynucleotides that have 95-99% homology to SEQ ID NO: 113 or the full-length cDNA or fragments of SEQ ID NO: 113 nor polynucleotides which hybridize to any of the above and still retain the recited property of SEQ ID NO: 113.

Applicants discuss the legal standards applied when evaluating Written Description, including the requirement that written description depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure (pages 8, 26 September 2005). The examiner takes no issue with the discussion of general requirements for evaluating Written Description in this case. However, Applicants have not described or shown possession of any polynucleotides 95-99% homologous to SEQ ID NO: 113 or the full-length cDNA or fragments of SEQ ID

NO: 113 nor polynucleotides which hybridize to any of the above, which has a "higher expression in normal stomach tissue compared to stomach tumor", except SEQ ID NO: 113. Nor have Applicants described a representative number of species that have 95-99% homology to SEQ ID NO: 113, such that it is clear that they were in possession of a genus of polynucleotides functionally similar to SEQ ID NO: 113. What is disclosed is a single species.

As discussed in the previous Office Actions (07 February 2005 and 25 July 2005) even a very skilled artisan could not envision the detailed chemical structure of all or a significant number of encompassed polynucleotides, and therefore, would not know how to make or use them. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making. The claimed product itself is required. Recitation of the phrase "wherein the isolated nucleic acid is more highly expressed in normal stomach tissues compared to stomach tumor tissue or wherein isolated nucleic acid molecule is suitable for use as PCR primer or probe," (amended claims, 21 May 2005), is not adequate to describe polynucleotides of the instant invention that have 95-99% homology to the SEQ ID NO: 113 or the full-length cDNA or fragments of SEQ ID NO: 113 nor polynucleotides which hybridize to any of the above, since there was no reduction to practice to support the amended claims. Specifically, there is no way of knowing which, if any variants would have the same property of higher expression in the specific tissues. There is no nexus between the degree of homology and "higher expression in normal stomach tissue compared to stomach" tumor. Until one identifies a particular variant that is highly expressed or not,

one of skilled in the art would not know the expression profile of the variant. The mere sequence alone will not allow one of skilled in the art to predict expression. Applicants made no variant polypeptides, and as recited in the current Written Description Guidelines, Applicants must have invented the subject matter that is claimed and must be in "possession" of the claimed genus (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Applicants argue (pages 9-10) that if there are sufficient identifying characteristics, *e.g.*, functional recitation coupled to a structure, there is sufficient written description. The argument has been fully considered, but is not persuasive. In the instant application the recitation provided (higher expression of SEQ ID NO: 113 in normal stomach compared to stomach tumor) is not a function but a property. The point is that **not** all polynucleotides with required structural relatedness and the limitation of being a probe or primer is not a sufficiently identifying feature. The specification does not convey to one of skill in the art, including recombinant DNA/protein technology art that the inventors were in possession of these non-identical occurring claimed polynucleotides. The specification does not provide information so the skilled artisan could readily envision such nucleic acids.

Applicants argue at pages 9-10 that there is sufficient written description for those claimed nucleic acids not identical to SEQ ID NO: 113 with no functional limitation specified, and that the finding in the *Enzo* case support the claimed invention having adequate written description. This argument has been fully considered but is not deemed persuasive because (a) the fact situation in the *Enzo* case is substantively

different from that in the instant case. The *Enzo* claims are drawn to a "composition of matter that is specific for *Neisseria gonorrhoeae",* which is then further described by ATCC deposit number and sequences that hybridize to such. It is further noted that the hybridization recitation in *Enzo* is substantively different than that herein, as it requires a comparative hybridization that demonstrates specificity of the claimed composition for one strain of *Neisseria* over another. By contrast, the instant claims have *no* functional limitations. Similarly, Example 9 of the Written Description Guidelines Training Materials is not applicable here, as the fact situation described therein is:

> The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

The nucleic acids claimed herein are not required to encode a protein, much less one with adenylate cyclase or other well-characterized activity. The fact situation therein is substantively different from that of the instant application. For these reasons and those previously of record, the rejection is maintained.

Appillvants also assert that by citing *In re Wallach* argue that the Examiner's premise that a large genus can not be adequately described a single species is simply wrong (see bottom of page 59-60). However, the fact pattern present in *In re Wallach* is different from instant invention. The claims were directed to polynucleotides sequences

encoding the polypeptide. However, the court affirmed the Board's determination (USPTO position) that the specification of the patent application did not provide an adequate written description of the pending claims. Appellants as in the instant application did not provide any evidence that there is any known or disclosed correlation between the combination of a partial structure of polynucleotides and the polynucleotides recited property.

In addition, Applicants citing the Written Description Guidelines of the U.S. Patent Office and argues that in Example 14, the procedures for making variants were known in the art and the disclosure taught how to test for claimed catalytic activity. Thus, it is asserted that written description requirement was found to be satisfied for claims relating to polypeptides having 95% homology to a particular sequence and possessing a particular catalytic activity, even though the Applicants had not made any variants. Applicants contend that similarly, the pending claims also have very high sequence homology to the disclosed sequences and must share the same expression pattern in certain tumors. The fact pattern in the instant application is not analogous to Example 14 in the Revised Interim Written Description Guidelines. In Example 14 of the Guidelines, the claimed protein variants have a high percent sequence identity in combination with a specific functional limitation. In the example, the protein catalyzes the reaction of A→B and thus, methods of generating variants of the protein that have 95% identity and retain its activity are conventional in the art because deletions, substitutions, insertions, and additions of uncritical amino acid residues would not affect the enzyme activity. Moreover, such an enzyme would have a conserved structure that

is responsible for the enzyme activity. Thus, it is likely predictable, based upon percent identity, which variant would share the same function. In contrast, in the instant case, polypeptide of PRO1446 has no utility and has no disclosed function. Furthermore, the specification and the claims do not disclose the identification of any particular portion of the PRO1446 structure that must be conserved in order to conserve the required function.

Applicants also argue (p. 13) that patents have been issued with claims to variant proteins and nucleic acids when such variants were never made. The argument has been fully considered, but is not persuasive. Each application is examined on its own merits.

Claim Rejections - 35 USC § 102 (new)

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (f) he did not himself invent the subject matter sought to be patented.

8a. Claims 4-6, 11-14, 16 and 21-27 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Based on Applicants provisional application (60/101475) disclosure, it appears that the instant cDNA is derived from the Incyte EST clone No. 2380344 (Appendix A, enclosed). Applicant states that "In light of the sequence homology between the DNA56514 sequence and the Incyte EST 2380344, the clone including this EST was purchased and the cDNA insert was

obtained and sequenced. The sequence of this cDNA insert is shown in Figure 2 and is herein designated as DNA71277-1636." Therefore, claims 4-6, 11-14, 16 and 21-27 rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Claim Rejections - 35 USC § 103, new

9. Claims 17-20 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over DNA56514 (appendix A) in view of Jacobs et al. (U.S. Patent No: 5 965 397).

The teachings of DNA69590 have been described above in paragraph 18. However, this DNA69590 does not teach vector and host cells.

Jacobs et al. teaches a vector comprising the cDNA, a host cell thereof (claims 1-4 and columns 19, 20, 24, lines: 31-65). Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to obtain vectors (with control sequences) containing DNA sequences and transfecting them into host cells as taught by Jacobs et al. by cloning the cDNA that generates a polypeptide, that is at least 99% identical to SEQ ID NO: 117 of the instant invention from DNA described by DNA69590. Further, Jacobs et al. have described the expression of nucleotides containing vectors with promoter sequences in bacterial hosts (columns 23-25).

The person of ordinary skill in the art would have been motivated to clone the nucleotide sequences described by DNA69590 because it would allow for the

expression of the polynucleotide and the subsequent characterization of the polypeptide. There is a reasonable expectation of success because transfecting the expression vector into host cell for the expression is routine in the art for expression studies and screen for new polypeptide. Therefore, the claims 16-20 and 28-31 are rejected as obvious over DNA69590 in view of in view of Jacobs et al. (U.S. Patent No: 5 965 397).

Conclusion

10. No claims are allowed.

Contact information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 3/06

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud

Appendix A Applicants copy

pancreatic islet cell library. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; http://bozeman.mbt.washington.edu/phrap.docs/phrap.html). The consensus sequence obtained therefrom is shown in Figure 4, and is herein designated DNA56514. In light of the sequence homology between the DNA56514 sequence and the Incyte EST 2380344, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 2 and is herein designated as DNA71277-1636.

The full length clone shown in Figure 2 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 152-154 and ending at the stop codon found at nucleotide positions 479-481 (Figure 2; SEQ ID NO:2). The predicted polypeptide precursor (Figure 1, SEQ ID NO:1) is 109 amino acids long with a signal peptide at about amino acids 1-15 of SEQ ID NO:1. PRO1446 has a calculated molecular weight of approximately 11822 daltons and an estimated pI of approximately 8.63. Clone DNA71277-1636 (UNQ740), designated as DNA71277-1636 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. _____.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 1 (SEQ ID NO:1), revealed sequence identity between the PRO1446 amino acid sequence and the following Dayhoff sequences (data incorporated herein): P53_CANFA, P53_FELCA, LRP1_HSV1F, OSU57338_1, S75842, P_P93722, AF002189_1, B70408, S54309 and S53365. The first in this list is further described in Kraegel, et al., Cancer Lett., 92(2):181-186 (1995).